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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 22428 | 7590 | 11/06/2003 | EXAMINER | |
| FOLEY AND LARDNER | | | YU, MISOOK | |
| SUITE 500 | | | ART UNIT | PAPER NUMBER |
| 3000 K STREET NW | | | | |
| WASHINGTON, DC 20007 | | | 1642 | |

DATE MAILED: 11/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|------------------------------|------------------|
| Office Action Summary | Application N . | Applicant(s) |
| | 09/509,775 | FUJITA, JUN |
| | Examiner MISOOK YU, Ph.D. | Art Unit 1642 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 11 August 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

4) Claim(s) 1 and 5-35 is/are pending in the application.

4a) Of the above claim(s) 6-15 and 18-34 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1,5,16,17 and 35 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>25</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Election/Restrictions

Claims 1 and 5-35 are pending.

Claims 6-15 and 18-34 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 5, 16, 17, and 35 are examined on merits.

Claim Objections

Claim 16 remain objected for reason of record and claim 17 are newly objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Applicant states, at the second last paragraph of page 6 of the amendment filed on 80/11/2003, "Applicant is not sure why the Examiner is asking a question about claim 16 in this rejection...." The Office assumes that the paragraph is the applicant's response to the objection of claim 16 although applicant's mention about "this rejection" at the last sentence of the paragraph is confusing. The protein in the base claim (claim 1) is limited to a protein with a specific sequence i.e., consisting of amino acid position #14 to SEQ ID NO:2. "Consisting of" something means only that something, no more, nothing else. However, the dependent claims are drawn to proteins that do not consist of amino acid position #14-226 of SEQ ID NO:2. Dependent claims are claims within

the scope of the base claim. However, the instant dependent claims are not within the scope of the base claim. If applicant is having difficulty with transitional phrases, then note MPEP 2111.03. For the purpose of this Office action, the Office will consider the limitations of each of the dependent claims as they are currently presented. However, this treatment does not relieve applicant the burden of responding this objection.

Claim Rejections - 35 USC § 112

Claims 1, 16, and 17 remain rejected for reason of record under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant does not address what the metes and bounds of the limitation “a signal sequence”. Although a signal sequence is well known in the art, the issues raised are whether the residues 1 to 13 of SEQ ID NO:2 is a signal peptide, and why a signal sequence is excluded in base claim 1 but include in dependent claim 16.

Claim 1 is newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 1 is drawn to a polypeptide consisting of amino acid #14 to #226 of SEQ ID NO:2 having biological activity of gankyrin. The specification at Example 4 (pages 55-58) discloses that the various biological activities of gankyrin is the characteristics of the SEQ ID NO:2, which is encoded by the 678-bp cDNA isolated in

Example 1 (pages 45-48). Note line 16-35 of page 55. The specification does not teach SEQ ID NO:2 lacking the first 13 amino acids has gankyrin biological activity.

Protein chemistry is unpredictable in the current state of art. For example, Wang, J. et al. 2000 J. Biol. Chem. 275 (1): 507-513 provide evidence that even a single amino acid change in a protein converts in vivo activity in unpredictable way (see Table 1). Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 1988,

8:1247-1252) teach that conservative substitutions in a protein do not lead to retaining biological activity of a protein. Lazar et al teach that transforming growth factor alpha, replacement of aspartic acid at position 47 with non-conservative residue alanine did not affect biological activity while replacement with a conservative residue, glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or "conservative" amino acid substitution in a protein will often dramatically affect the biological activity and characteristics of a protein.

Considering the state of art and the limited teachings of the specification, it is concluded that undue experimentation would be required to practice the invention.

Claim Rejections - 35 USC § 102

Claims 5 and 35 **remain rejected** for reason of record under 35 U.S.C. 102(b) as being anticipated by Kato et al (IDS, JP 9-75085, published 25 March 1997).

The rejection of Claim 1 is withdrawn because the amended claim 1 is drawn to the polypeptide consisting of amino acid #14 to #226 of SEQ ID NO:2.

Applicant appears to argue that the art does not teach the polypeptide consisting of amino acid #14 to #226 of SEQ ID NO:2 but this argument is not commensurate in scope of claims because claims 5 and 25 are not limited to the polypeptide consisting of amino acid #14 to #226 of SEQ ID NO:2 but drawn to a polypeptide encoded by DNA molecule hybridizing to instant SEQ ID NO:1. Since the protein of art is 100 % identical to instant SEQ ID NO:2 and the specification at Example 4 (pages 55-58) discloses that the various biological activities of gankyrin listed in instant claim 5 is the characteristics

of the SEQ ID NO:2, which is encoded by the 678-bp cDNA isolated in Example 1 (pages 45-48), the claims are anticipated by Kato et al.

Claim Rejections - 35 USC § 103

Claims 16 and 17 remain rejected for reason of record under 35 U.S.C. 103(a) as being unpatentable over Kato (IDS, JP 9-75085, published 25 March 1997) as applied to claims 5 and 35 above, and further in view of Zhang et al (1995, a copy provided in the previous Office action) and Jamsa et al (1995, a copy provided in the previous Office action).

Applicant appears to argue that the amended claim 1 is limited to specific fragment of SEQ ID NO:2, therefore no motivation in the art to combine references to arrive at the invention. However, the claims as currently presented are not limited to the specific fragment recited in the base claim. Claims 16 and 17 appear to read on the protein taught by Kato et al because claim 1 appears to say that amino acid position 1-13 of SEQ ID NO:2 is a signal sequence and claim 16 is adding said signal sequence back. Neither the specification nor applicant's argument/response has defined the scope of the claim 16 or what is meant by a signal sequence. When the claims are limited to the specific fragment recited in the base claim, this rejection would be withdrawn.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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Art Unit: 1642

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Misook Yu

October 30, 2003

Mary E. Mosher
PRIMARY EXAMINER
GROUP 1800-1600